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TITLE OF INVENTION: CUSTOM VECTORS FOR TREATING AND PREVENTING PANCREATIC CANCER

APPLICANT FOR DO/US: THERION BIOLOGICS CORPORATION, et al.

CERTIFICATE OF FACSIMILE

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Date: October 25, 2005

Linda M. Ginsberg

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Fax 011-41-22 338.90.90

LETTER ACCOMPANYING ARTICLE 34(2)(B) AMENDMENTS

Dear Sir/Madam:

Pursuant to Patent Cooperation Treaty Article 43(2)(b) and Rule 66.8, applicants request that pages 73-76 of the above-identified international application be replaced with attached replacement sheets pages 73-77.

The differences between the claims as filed and the claims as amended are as follows:

Claims 1 – 25 are unchanged.

New claims 26 – 44 are added.

Applicants respectfully submit that these claims, as amended, do not go beyond the disclosure in the International Application as filed, and their entry is respectfully requested. See for example, pages 15-18 and Figures 7-12.

Date: October 25, 2005

Respectfully submitted,

Ronald I. Eisenstein (Reg. No. 30,628)
NIXON PEABODY LLP
100 Summer Street
Boston, MA 02110
(617) 345-6054

We claim:

1. A method for inducing an immunological response against a malignant pancreatic cell in an individual, said method comprising the steps of: selecting an individual having malignant pancreatic cells or at risk for developing such a pancreatic tumor, administering to the individual a first vector containing a first gene, or antigenic portion thereof, that encodes a pancreatic tumor-associated antigen (PTAA), and at regular intervals thereafter administering at least a second vector containing a gene encoding PTAA or antigenic portion thereof, wherein if CEA or MUC-1 or an antigenic portion thereof or a modified version thereof is the PTAA, there must be a second PTAA present.
2. The method of claim 1, further comprising administering granulocyte-macrophage colony stimulating factor (GM-CSF).
3. The method of claim 1 or 2, further comprising administering at least one co-stimulatory molecule.
4. The method of claim 3, wherein the co-stimulatory molecule is administered as a gene contained within the same vector as the vector containing gene encoding the PTAA.
5. The method of claim 3, wherein the co-stimulatory molecule is administered as a gene contained within a different vector than the vector containing gene encoding the PTAA.
6. The method according to claims 1-5, wherein said PTAA, or antigenic portion thereof, is contained in a poxvirus vector.
7. The method according to claim 7, wherein said poxvirus vector is selected from the group consisting of an orthopox virus vector; avipox virus vector; a suipox virus vector; a capripox virus vector; a leporipox virus vector; and an iridovirus vector.
8. The method according to claim 6, wherein said pox virus vector is a replication impaired or non-replicating pox virus vector.
9. The method according to claim 8, wherein said pox virus vector is an orthopox vector.
10. The method according to claim 9, wherein said orthopox virus vector is vaccinia.

11. The method of claims 1-10, wherein the PTAA is selected from the group consisting of carcinoembryonic antigen, mucin, ras, gastrin, erbB2, interferonα, tumor necrosis factor-α, hMP-9 immunotoxin, antigenic portions thereof, and modified versions thereof.

12. The method of claim 11, wherein the PTAA is a mucin selected from the group consisting of MUC-1, MUC-2, MUC-3, MUC-4, MUC-5AC, MUC-5B, MUC-6, MUC-7, MUC-11, MUC-12, and antigenic portions thereof and modified versions thereof.

13. The method of claim 11, wherein the modified version thereof is wobbled-MUC.

14. The method of claims 1-11, wherein the vectors contain genes encoding at least two PTAAs or antigenic portions thereof.

15. The method of claim 14, wherein the PTAA is CEA and a mucin.

16. The method of claim 15, wherein the mucin is wobbled MUC-1 or wobbled mini-MUC.

17. The method of claims 1-16, wherein one to three administrations at set intervals are made by an orthopox vector containing the at least one PTAA or antigenic portion thereof and multiple administrations at set intervals are made by an avipox vector containing the at least one PTAA or antigenic portion thereof.

18. The method of claim 17, wherein the orthopox vector is vaccinia.

19. The method of claim 18, wherein the vaccinia is an attenuated vaccinia.

20. The method of claim 19, wherein the attenuated vaccinia is MVA or NYVAC.

21. The method of claims 17, 18, 19 or 20, wherein the orthopox vector is administered before the avipox vector is administered.

22. The method of claim 21, wherein the set interval is 20 days to 90 days.

23. A kit for enhancing a protective immune reaction against a pancreatic tumor comprising at least one pox vector encoding at least two PTAAs or antigenic portion thereof.

24. The kit of claim 23, wherein one PTAA is CEA and the at least second PTAA is MUC-1 or mini-MUC.

25. The kit of claim 24, wherein mini-MUC contains six tandem repeats, is wobbled at the nucleic acid level to prevent excision during homologous recombination, and may further contain additional mutations to enhance immunogenicity.

26. An isolated nucleic acid molecule encoding a Muc-1 fragment sufficient to generate an immune reaction to Muc-1.

27. The isolated nucleic acid molecule of claim 26, wherein the Muc-1 fragment will not undergo extensive excision as a result of homologous recombination.

28. The isolated nucleic acid molecule of claim 26, wherein the Muc-1 fragment comprises from between about 5 to about 25 Muc-1 tandem repeat units.

29. The isolated nucleic acid molecule of claim 26, wherein the Muc-1 fragment comprises from between about 6 to about 15 Muc-1 tandem repeat units.

30. The isolated nucleic acid molecule of claim 26, wherein the Muc-1 fragment comprises from between about 6 to about 12 Muc-1 tandem repeat units.

31. The isolated nucleic acid molecule of claim 26, wherein the Muc-1 fragment comprises about 6 Muc-1 tandem repeat units.

32. The isolated nucleic acid molecule of claim 26, wherein the Muc-1 fragment is wobbled.

33. An isolated nucleic acid molecule encoding one or more of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, or SEQ ID NO:4, or a fragment or variant thereof.

34. A method for inducing an immunological response against a malignant pancreatic cell in an individual, comprising administering a therapeutically effective amount of a nucleic acid molecule encoding a Muc-1 fragment sufficient to generate an immune reaction to Muc-1.

35. The method of claim 34, wherein the Muc-1 fragment will not undergo extensive excision as a result of homologous recombination.

36. The method of claim 34, wherein the Muc-1 fragment comprises from between about 5 to about 25 Muc-1 tandem repeat units.

37. The method of claim 34, wherein the Muc-1 fragment comprises from between about 6 to about 15 Muc-1 tandem repeat units.

38. The method of claim 34, wherein the Muc-1 fragment comprises from between about 6 to about 12 Muc-1 tandem repeat units.

39. The method of claim 34, wherein the Muc-1 fragment comprises about 6 Muc-1 tandem repeat units.

40. The method of claim 34, wherein the Muc-1 fragment is wobbled.

41. A method for inducing an immunological response against a malignant pancreatic cell in an individual, comprising administering a therapeutically effective amount of one or more of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, or SEQ ID NO:4, or a fragment or variant thereof.

42. A kit for enhancing a protective immune reaction against a pancreatic tumor comprising one or more of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, or SEQ ID NO:4, or a fragment or variant thereof and instructions for use.

43. A kit for enhancing a protective immune reaction against a pancreatic tumor comprising one or more of an isolated nucleic acid molecule encoding a Muc-1 fragment sufficient to generate an immune reaction to Muc-1 and instructions for use.

44. The kit of claim 43, wherein the Muc-1 fragment comprises from between about 5 to about 25 Muc-1 tandem repeat units.

ABSTRACT

The present invention is directed to a system for treating individuals at risk of developing or suffering from pancreatic cancer. The system comprises administering to the individual a recombinant poxvirus, where the poxvirus contains a foreign nucleic acid encoding at least one pancreatic tumor associated antigen (PTAA).